

VAR G1=O/N
VPA 19-2/1/5/4 U
ENTER (DIS), GRA, NOD, BON OR ?:end
L1 STRUCTURE CREATED

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SAMPLE SCREEN SEARCH COMPLETED - 101 TO ITERATE

100.0% PROCESSED 101 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1418 TO 2622
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

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SEARCH TIME: 00.00.01

L3 5 SEA SSS FUL L1

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ENTRY SESSION
FULL ESTIMATED COST 156.68 156.89

FILE 'CAPLUS' ENTERED AT 09:48:46 ON 26 JUL 2004
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FILE COVERS 1907 - 26 Jul 2004 VOL 141 ISS 5

FILE LAST UPDATED: 25 Jul 2004 (20040725/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 1 L3

=> d bib abs hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:80652 CAPLUS

DN 140:146007

TI Preparation of piperidinyketones as selective inhibitors of macrophage inflammatory protein 1 α (MIP-1 α) binding to CCR1 chemokine receptors.

IN Blumberg, Laura Cook; Brown, Matthew Frank; Hayward, Matthew Merrill; Poss, Christopher Stanley

PA Pfizer Products Inc., USA

SO PCT Int. Appl., 62 pp.

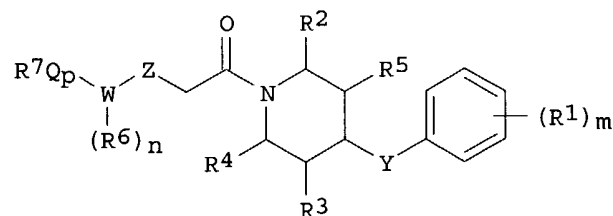
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|-----------------|----------|
| PI | WO 2004009550 | A1 | 20040129 | WO 2003-IB2876 | 20030707 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
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| | US 2004063759 | A1 | 20040401 | US 2003-616844 | 20030708 |
| PRAI | US 2002-397108P | P | 20020718 | | |
| OS | MARPAT 140:146007 | | | | |
| GI | | | | | |



I

AB Title compds. [I; m = 1-5; n = 0-4; p = 0-1; Q = alkyl; W = aryl, heteroaryl; Y = O, NR⁸; R⁸ = H, alkyl; Z = O, NR⁹; R⁹ = H, alkyl, Ac; R¹ = H, halo, cyano, NO₂, CF₃, OCF₃, alkyl, OH, alkylcarbonyloxy, alkoxy; R²-R⁵ = H, (halo)alkyl; R⁶ = H, halo, (halo)alkyl, cyano, alkoxy, aminocarbonyl, carboxy, alkylcarbonyl, (halo)alkoxy; R⁷ = H, halo, (halo)alkyl, dialkylaminoalkylaminocarbonyl, alkoxy, aminocarbonyl, ureido, aminosulfonyl, alkylsulfonylaminoalkylamino, aminosulfonylamino, heteroaryloxy, ureidoalkylaminocarbonyl, etc.; ≥ 1 of R²-R⁵ =

alkyl], were prepared Thus, 2-(2-amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone (preparation given) in CH₂Cl₂ was treated with Et₃N and Ph chloroformate, The reaction was stirred at ambient temperature for 4 h, concentrated in vacuo, and the resulting residue dissolved in methanol followed by bubbling in ammonia gas for 10 min and stirred overnight at ambient temperature to give

[5-chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea. I inhibited chemotaxis with IC₅₀ <10 μM.

IT 651301-01-8P

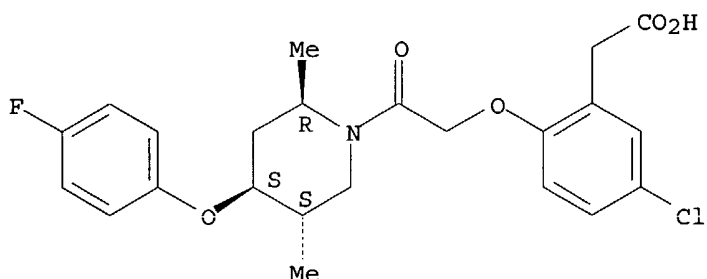
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of piperidinyketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651301-01-8 CAPLUS

CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 651300-98-0P 651301-03-0P 651301-04-1P

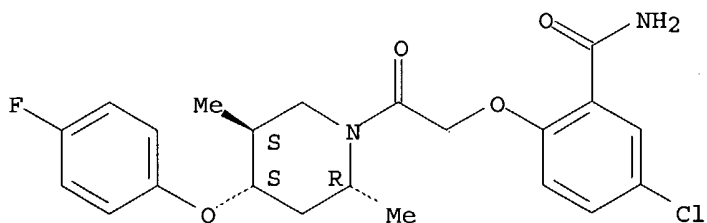
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidinyketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651300-98-0 CAPLUS

CN Benzamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

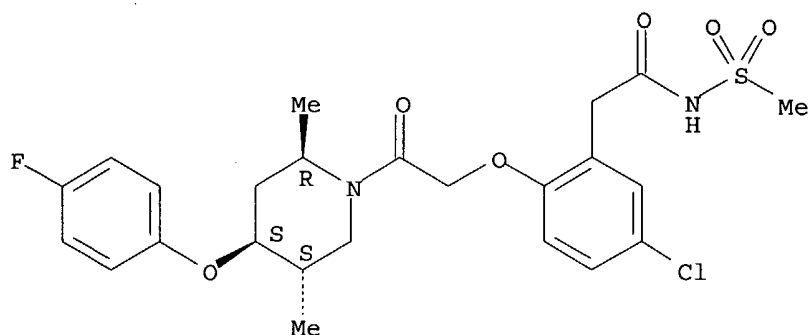
Relative stereochemistry.



RN 651301-03-0 CAPLUS

CN Benzeneacetamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-N-(methylsulfonyl)-, rel- (9CI) (CA INDEX NAME)

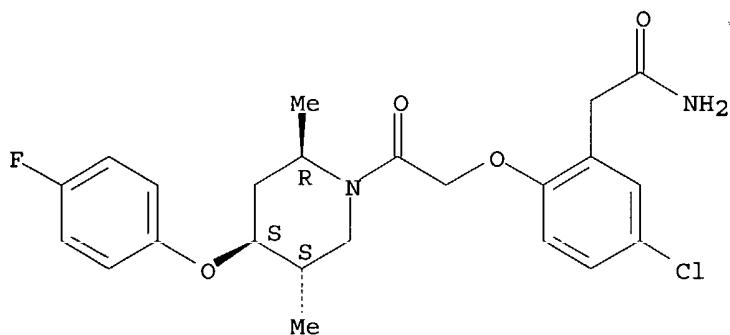
Relative stereochemistry.



RN 651301-04-1 CAPLUS

CN Benzeneacetamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 651301-33-6P

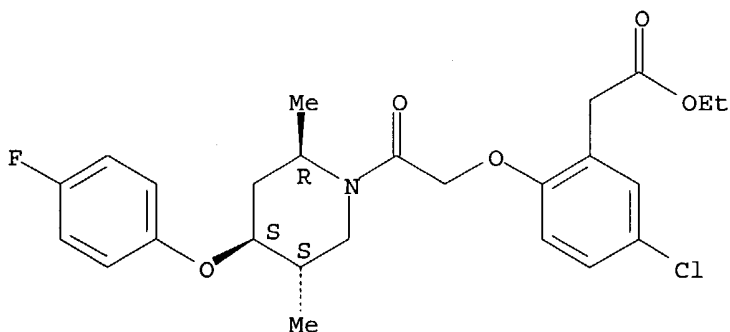
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1 α (MIP-1 α) binding to CCR1 chemokine receptors)

RN 651301-33-6 CAPLUS

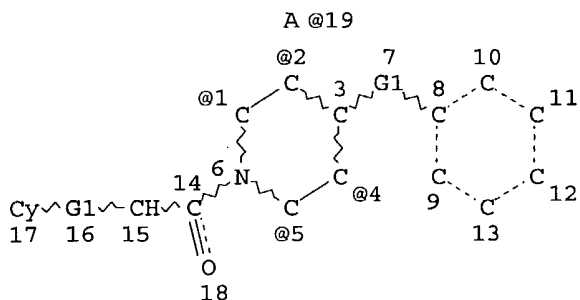
CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT



VAR G1=O/N
VPA 19-2/1/5/4 U
ENTER (DIS), GRA, NOD, BON OR ?:end
L1 STRUCTURE CREATED

=> s l1
SAMPLE SEARCH INITIATED 09:48:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 101 TO ITERATE

100.0% PROCESSED 101 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1418 TO 2622
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

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FULL SEARCH INITIATED 09:48:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2049 TO ITERATE

100.0% PROCESSED 2049 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

L3 5 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 156.68 156.89

FILE 'CAPLUS' ENTERED AT 09:48:46 ON 26 JUL 2004
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FILE COVERS 1907 - 26 Jul 2004 VOL 141 ISS 5

FILE LAST UPDATED: 25 Jul 2004 (20040725/ED)

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=> s l3

L4 1 L3

=> d bib abs hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:80652 CAPLUS

DN 140:146007

TI Preparation of piperidinylketones as selective inhibitors of macrophage inflammatory protein 1 α (MIP-1 α) binding to CCR1 chemokine receptors.

IN Blumberg, Laura Cook; Brown, Matthew Frank; Hayward, Matthew Merrill; Poss, Christopher Stanley

PA Pfizer Products Inc., USA

SO PCT Int. Appl., 62 pp.

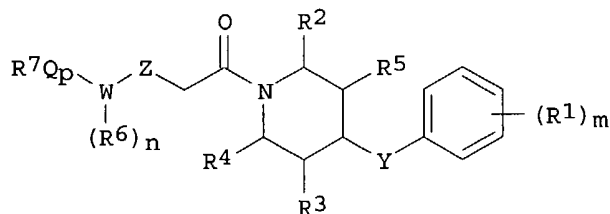
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| PI | WO 2004009550 | A1 | 20040129 | WO 2003-IB2876 | 20030707 |
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| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 2004063759 | A1 | 20040401 | US 2003-616844 | 20030708 |
| PRAI | US 2002-397108P | P | 20020718 | | |
| OS | MARPAT 140:146007 | | | | |
| GI | | | | | |



I

AB Title compds. [I; m = 1-5; n = 0-4; p = 0-1; Q = alkyl; W = aryl, heteroaryl; Y = O, NR8; R8 = H, alkyl; Z = O, NR9; R9 = H, alkyl, Ac; R1 = H, halo, cyano, NO2, CF3, OCF3, alkyl, OH, alkylcarbonyloxy, alkoxy; R2-R5 = H, (halo)alkyl; R6 = H, halo, (halo)alkyl, cyano, alkoxy, aminocarbonyl, carboxy, alkylcarbonyl, (halo)alkoxy; R7 = H, halo, (halo)alkyl, dialkylaminoalkylaminocarbonyl, alkoxy, aminocarbonyl, ureido, aminosulfonyl, alkylsulfonylaminoalkylamino, aminosulfonylamino, heteroaryloxy, ureidoalkylaminocarbonyl, etc.; ≥ 1 of R2-R5 =

alkyl], were prepared Thus, 2-(2-amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone (preparation given) in CH₂Cl₂ was treated with Et₃N and Ph chloroformate, The reaction was stirred at ambient temperature for 4 h, concentrated in vacuo, and the resulting residue dissolved in methanol followed by bubbling in ammonia gas for 10 min and stirred overnight at ambient temperature to give

[5-chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea. I inhibited chemotaxis with IC₅₀ <10 µM.

IT 651301-01-8P

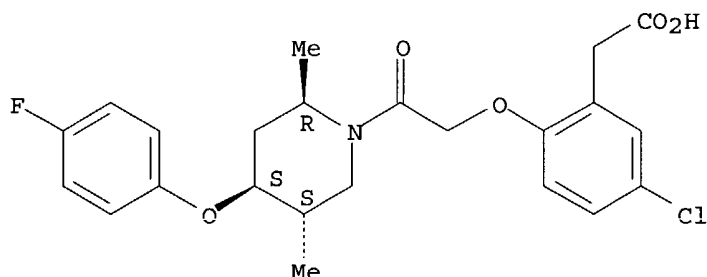
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(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651301-01-8 CAPLUS

CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 651300-98-0P 651301-03-0P 651301-04-1P

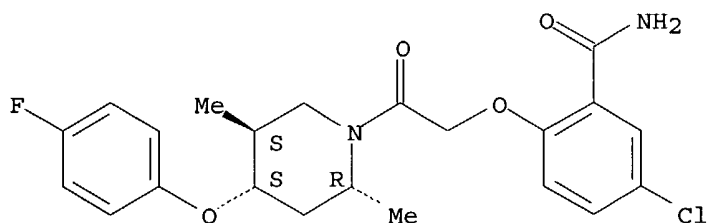
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651300-98-0 CAPLUS

CN Benzamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

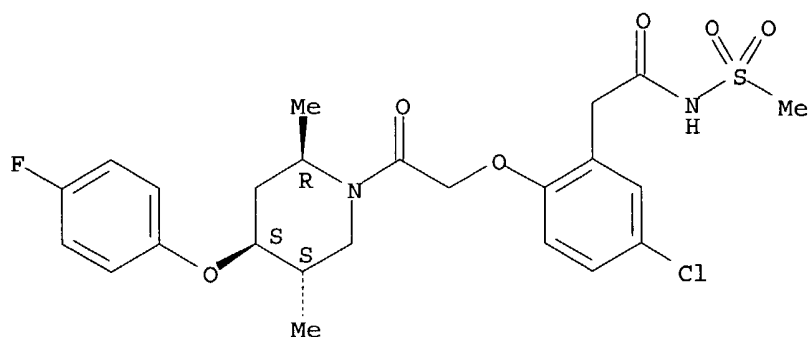
Relative stereochemistry.



RN 651301-03-0 CAPLUS

CN Benzeneacetamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-N-(methylsulfonyl)-, rel- (9CI) (CA INDEX NAME)

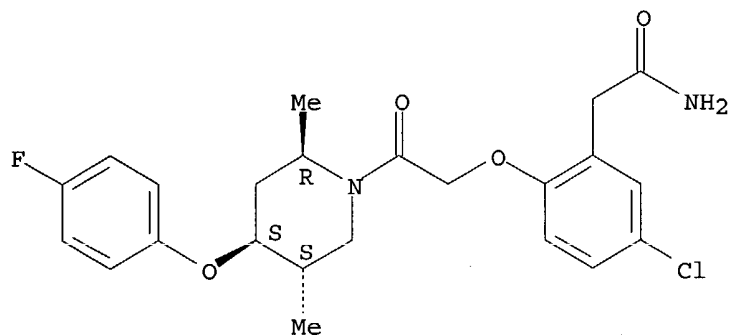
Relative stereochemistry.



RN 651301-04-1 CAPLUS

CN Benzeneacetamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 651301-33-6P

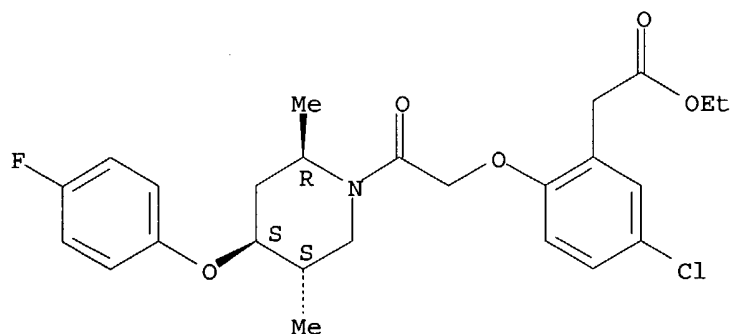
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1 α (MIP-1 α) binding to CCR1 chemokine receptors)

RN 651301-33-6 CAPLUS

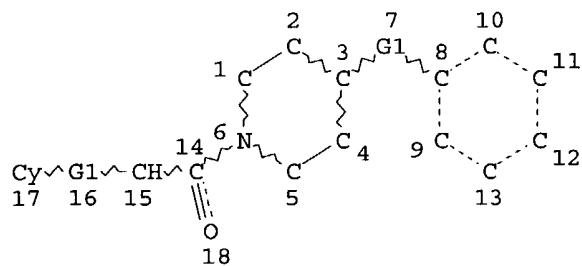
CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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 L5 HAS NO ANSWERS
 L5 STR



VAR G1=O/N
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RSPEC 2 8
 NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

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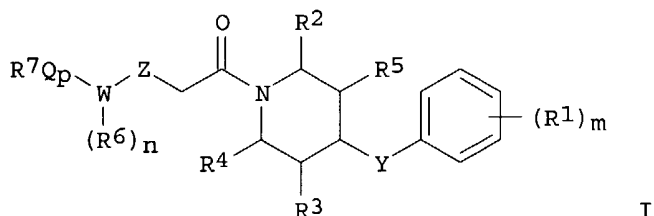
26 ANSWERS

L8 26 SEA SSS FUL L5

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L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2004:80652 CAPLUS
 DN 140:146007
 TI Preparation of piperidinyketones as selective inhibitors of macrophage inflammatory protein 1 α (MIP-1 α) binding to CCR1 chemokine receptors.
 IN Blumberg, Laura Cook; Brown, Matthew Frank; Hayward, Matthew Merrill; Poss, Christopher Stanley
 PA Pfizer Products Inc., USA
 SO PCT Int. Appl., 62 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004009550 | A1 | 20040129 | WO 2003-IB2876 | 20030707 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2004063759 | A1 | 20040401 | US 2003-616844 | 20030708 |
| PRAI | US 2002-397108P | P | 20020718 | | |
| OS | MARPAT 140:146007 | | | | |
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AB Title compds. [I; m = 1-5; n = 0-4; p = 0-1; Q = alkyl; W = aryl, heteroaryl; Y = O, NR8; R8 = H, alkyl; Z = O, NR9; R9 = H, alkyl, Ac; R1 = H, halo, cyano, NO2, CF3, OCF3, alkyl, OH, alkylcarbonyloxy, alkoxy; R2-R5 = H, (halo)alkyl; R6 = H, halo, (halo)alkyl, cyano, alkoxy, aminocarbonyl, carboxy, alkylcarbonyl, (halo)alkoxy; R7 = H, halo, (halo)alkyl, dialkylaminoalkylaminocarbonyl, alkoxy, aminocarbonyl, ureido, aminosulfonyl, alkylsulfonylaminoalkylamino, aminosulfonylamino, heteroaryloxy, ureidoalkylaminocarbonyl, etc.; ≥ 1 of R2-R5 = alkyl], were prepared Thus, 2-(2-amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone (preparation given) in CH2Cl2 was treated with Et3N and Ph chloroformate, The reaction was stirred at ambient temperature for 4 h, concentrated in vacuo, and the resulting residue dissolved in methanol followed by bubbling in ammonia gas for 10 min and stirred overnight at ambient temperature to give [5-chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea. I inhibited chemotaxis with IC50 <10 μ M.

IT **651300-89-9P**, 2-(4-Chlorophenoxy)-1-(4-phenoxy)piperidin-1-yl)ethanone **651300-90-2P**, 2-(4-Chlorophenoxy)-1-[4-(4-

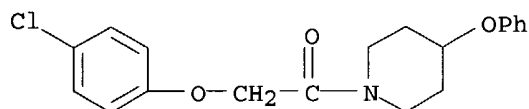
fluorophenoxy)piperidin-1-yl]ethanone **651300-92-4P**,
 5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]benzamide
651300-93-5P, [5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea **651301-05-2P**, [5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]acetic acid
651301-07-4P, N-[[5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidinyketones as as selective inhibitors of macrophage inflammatory protein 1 α (MIP-1 α) binding to CCR1 chemokine receptors)

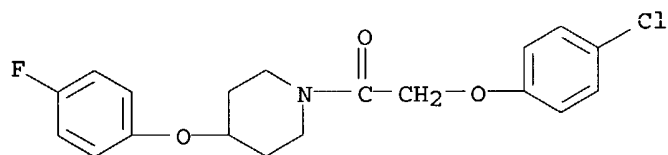
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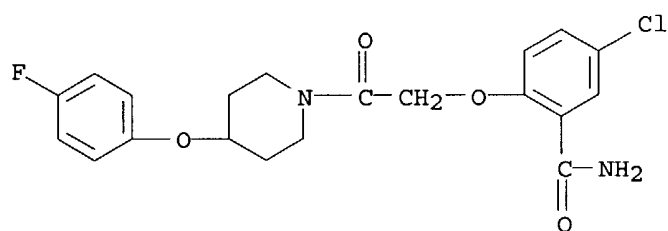
RN 651300-90-2 CAPLUS

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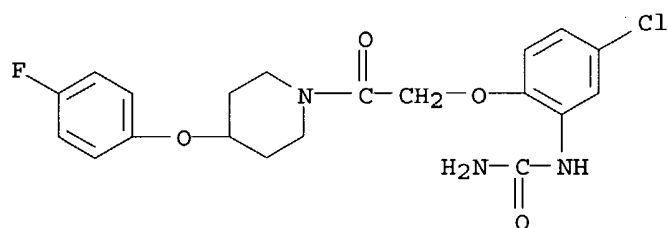
RN 651300-92-4 CAPLUS

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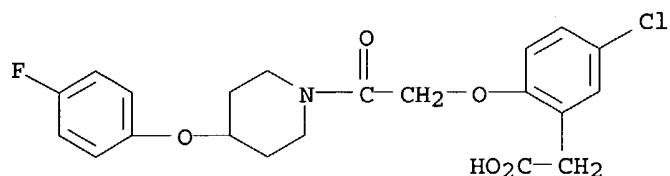


RN 651300-93-5 CAPLUS

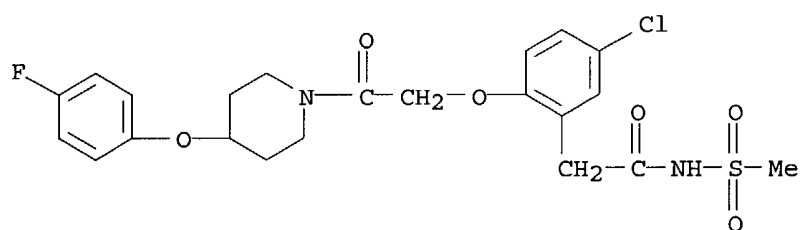
CN Piperidine, 1-[[2-[(aminocarbonyl)amino]-4-chlorophenoxy]acetyl]-4-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



RN 651301-05-2 CAPLUS
 CN Benzeneacetic acid, 5-chloro-2-[2-[4-(4-fluorophenoxy)-1-piperidinyl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

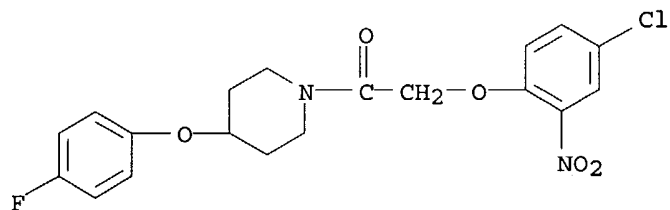


RN 651301-07-4 CAPLUS
 CN Benzeneacetamide, 5-chloro-2-[2-[4-(4-fluorophenoxy)-1-piperidinyl]-2-oxoethoxy]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)

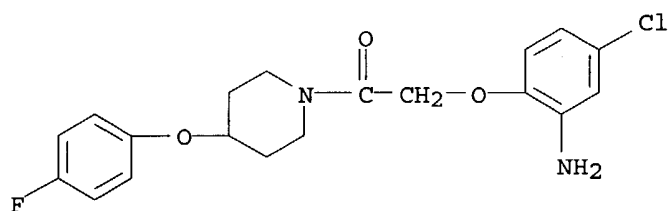


IT 651301-45-0P, 2-(4-Chloro-2-nitrophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone 651301-48-3P,
 2-(2-Amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of piperidinyllketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651301-45-0 CAPLUS
 CN Piperidine, 1-[(4-chloro-2-nitrophenoxy)acetyl]-4-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



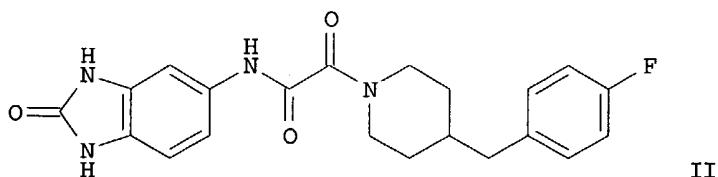
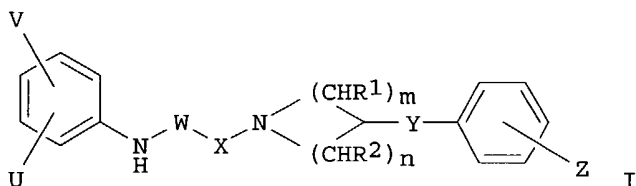
RN 651301-48-3 CAPLUS
 CN Piperidine, 1-[(2-amino-4-chlorophenoxy)acetyl]-4-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:97412 CAPLUS
DN 138:153539
TI Preparation of 2-(piperidin-1-yl)acetamides as NMDA receptor antagonists
IN Domany, Gyoergy; Horvath, Csilla; Farkas, Sandor; Barta Szalai, Gisella;
Nagy, Jozsef; Kolok, Sandor; Kovacs Bozo, Eva; Borza, Istvan; Vago,
Istvan; Bielik, Attila; Szendrei, Mrs. Gyorgyi Ignaczne; Keseru, Gyorgy
PA Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|-----------------|----------|
| PI | WO 2003010159 | A1 | 20030206 | WO 2002-HU71 | 20020723 |
| | WO 2003010159 | C1 | 20040212 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RQ, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | EE 200400058 | A | 20040415 | EE 2004-58 | 20020723 |
| | EP 1409477 | A1 | 20040421 | EP 2002-753161 | 20020723 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| PRAI | HU 2001-3055 | A | 20010724 | | |
| | HU 2002-2213 | A | 20020710 | | |
| | WO 2002-HU71 | W | 20020723 | | |
| OS | MARPAT 138:153539 | | | | |
| GI | | | | | |



AB The title compds. I [wherein V and U = independently H, halo, OH, CN, NO₂, NH₂, alkylsulfonyloxy, carboxyl, CF₃, CF₃O, alkyl-SO₂-NHCH₂, NH₂-(CH₂)₁₋₄-SO₂NH, NH₂-(CH₂)₁₋₄-CONH, sulfamoyl, CHO, aminomethyl, HOCH₂, alkyl, alkoxyethyl, halo-CH₂, tetrazolyl, alkoxy(carbonyl), alkanoyloxy,

Ph, (un)substituted alkylamino, arylamino, aralkylamino, alkylsulfonamido, alkanoylamido, arylsulfonamido, or alkoxy groups; or the neighboring V and U together form (un)substituted 4-7 membered ring with the atoms attached; W and X = independently CO, CH₂, or CH-alkyl; Y = O, (cyclo)alkylene, alkynylene, aminocarbonyl, NH, N-alkyl, CH₂O, CH(OH), or OCH₂; Z = H, halo, NO₂, NH₂, alkyl, alkoxy, CN, CF₃, OH, or CO₂H; R₁ and R₂ = independently H or alkyl; or R₁ and R₂ together form (un)substituted C₁-C₃ bridge; n and m = independently 0-3 with restriction that n and m ≠ 0 at the same time; with provisos] and optical antipodes, racemates, or pharmaceutically acceptable salts thereof are prepared as NMDA receptor antagonists, and moreover most of the compds. are selective antagonist of NR2B subtype of NMDA receptor. For example, 2-[4-(4-fluorobenzyl)piperidin-1-yl]-2-oxoacetic acid (prepn given) was treated with 5-amino-1,3-dihydroindol-2-one in DMF in the presence of Et₃N and HBTU to afford the acetamide II (48%). II showed IC₅₀ of 0.0007 μM against NMDA in rat. Formulations containing I as an active ingredient were also described.

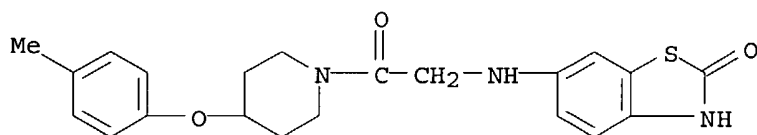
IT 496057-62-6P 496057-66-0P 496058-00-5P
496058-03-8P 496058-04-9P 496058-06-1P
496058-14-1P 496058-15-2P 496058-17-4P
496058-18-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(NMDA receptor antagonist; preparation of piperidinylacetamides by coupling reactions as NMDA receptor antagonists)

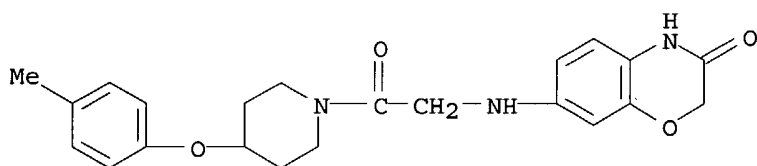
RN 496057-62-6 CAPLUS

CN Piperidine, 1-[[[(2,3-dihydro-2-oxo-6-benzothiazolyl)amino]acetyl]-4-(4-methylphenoxy)- (9CI) (CA INDEX NAME)



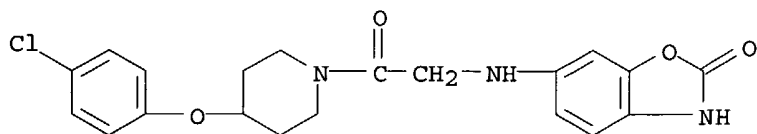
RN 496057-66-0 CAPLUS

CN Piperidine, 1-[[[(3,4-dihydro-3-oxo-2H-1,4-benzoxazin-7-yl)amino]acetyl]-4-(4-methylphenoxy)- (9CI) (CA INDEX NAME)



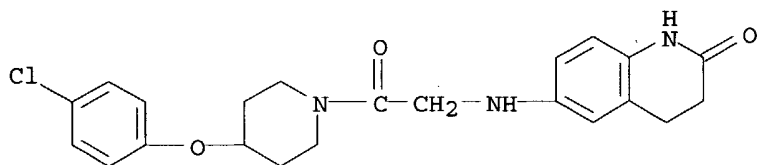
RN 496058-00-5 CAPLUS

CN Piperidine, 4-(4-chlorophenoxy)-1-[[[(2,3-dihydro-2-oxo-6-benzoxazolyl)amino]acetyl]- (9CI) (CA INDEX NAME)



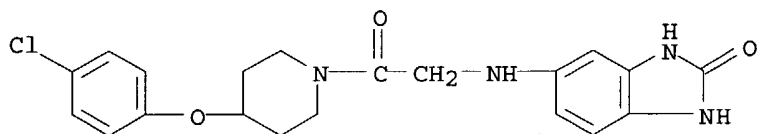
RN 496058-03-8 CAPLUS

CN Piperidine, 4-(4-chlorophenoxy)-1-[[[(1,2,3,4-tetrahydro-2-oxo-6-quinolinyl)amino]acetyl]- (9CI) (CA INDEX NAME)



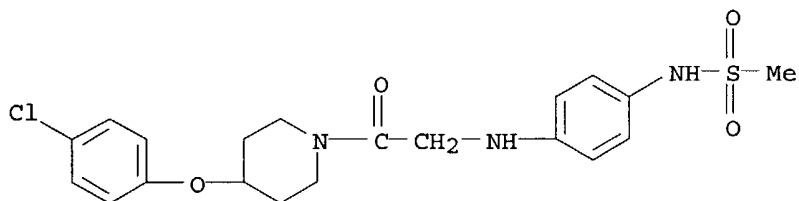
RN 496058-04-9 CAPLUS

CN Piperidine, 4-(4-chlorophenoxy)-1-[[[(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)amino]acetyl]- (9CI) (CA INDEX NAME)



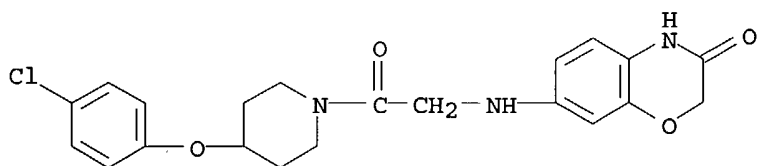
RN 496058-06-1 CAPLUS

CN Piperidine, 4-(4-chlorophenoxy)-1-[[[4-[(methylsulfonyl)amino]phenyl]amino]acetyl]- (9CI) (CA INDEX NAME)



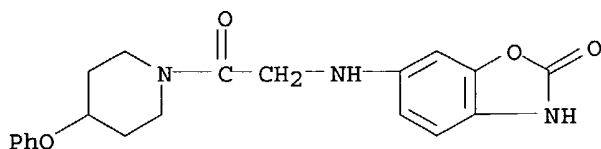
RN 496058-14-1 CAPLUS

CN Piperidine, 4-(4-chlorophenoxy)-1-[[[(3,4-dihydro-3-oxo-2H-1,4-benzoxazin-7-yl)amino]acetyl]- (9CI) (CA INDEX NAME)



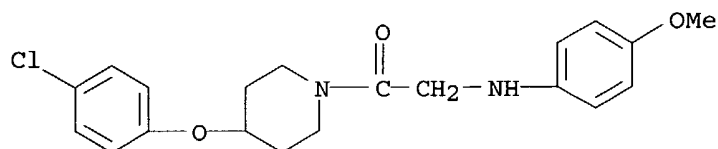
RN 496058-15-2 CAPLUS

CN Piperidine, 1-[[[(2,3-dihydro-2-oxo-6-benzoxazolyl)amino]acetyl]-4-phenoxy- (9CI) (CA INDEX NAME)



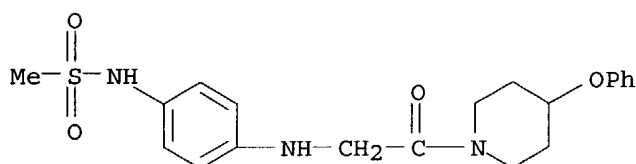
RN 496058-17-4 CAPLUS

CN Piperidine, 4-(4-chlorophenoxy)-1-[[4-(methoxyphenyl)amino]acetyl] - (9CI)
(CA INDEX NAME)



RN 496058-18-5 CAPLUS

CN Piperidine, 1-[[4-[(methylsulfonyl)amino]phenyl]amino]acetyl]-4-phenoxy-
(9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:589098 CAPLUS

DN 131:331730

TI Synthesis of a Series of 4-Benzyloxylaniline Analogs as Neuronal N-Type
Calcium Channel Blockers with Improved Anticonvulsant and Analgesic
Properties

AU Hu, Lain-Yen; Ryder, Todd R.; Rafferty, Michael F.; Feng, M. Rose;
Lotarski, Susan M.; Rock, David M.; Sinz, Michael; Stoehr, Sally J.;
Taylor, Charles P.; Weber, Mark L.; Bowersox, S. Scott; Miljanich, George
P.; Millerman, Elizabeth; Wang, Yong-Xiang; Szoke, Balazs G.

CS Departments of Chemistry Neuroscience Therapeutics and Pharmacokinetics
Dynamics and Metabolism, Parke-Davis Pharmaceutical Research Division of
Warner-Lambert Company, Ann Arbor, MI, 48105, USA

SO Journal of Medicinal Chemistry (1999), 42(20), 4239-4249
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB In this article, the rationale for the design, synthesis, and biol.
evaluation of a series of N-type voltage-sensitive calcium channel (VSCC)
blockers is described. N-Type VSCC blockers, such as ziconotide, have
shown utility in several models of stroke and pain. Modification of the
previously reported lead led to several 4-(4-benzyloxylphenyl)piperidine
structures with potent in vitro and in vivo activities. In this series,
the most interesting compound, (S)-2-amino-1-{4-[(4-benzyloxy-phenyl)-(3-
methyl-but-2-enyl)-amino]-piperidin-1-yl}-4-methyl-pentan-1-one (I),
blocked N-type calcium channels (IC₅₀ = 0.67 μM in the IMR32 assay) and
was efficacious in the audiogenic DBA/2 seizure mouse model (ED₅₀ = 6
mg/kg, i.v.) as well as the antiwrithing model (ED₅₀ = 6 mg/kg, i.v.).
Whole-cell voltage-clamp electrophysiol. expts. demonstrated that compound I
blocked N-type Ca²⁺ channels and Na⁺ channels in superior cervical
ganglion neurons at similar concns. Compound I, which showed superior in
vivo efficacy, stands out as an interesting lead for further development
of neurotherapeutic agents in this series.

IT 250237-03-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological

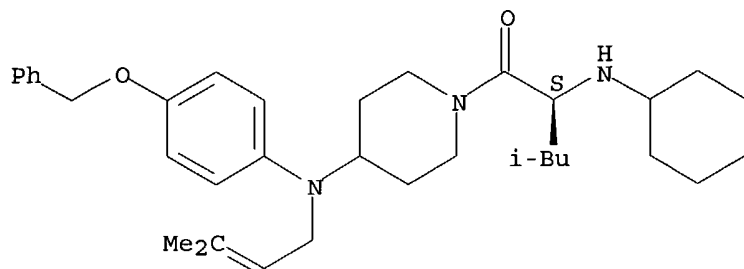
study); PREP (Preparation)

(synthesis of 4-benzyloxyaniline analogs as neuronal N-type calcium channel blockers with improved anticonvulsant and analgesic properties)

RN 250237-03-7 CAPLUS

CN 4-Piperidinamine, 1-[(2S)-2-(cyclohexylamino)-4-methyl-1-oxopentyl]-N-(3-methyl-2-butenyl)-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:126886 CAPLUS

DN 130:196584

TI Preparation of aniline derivatives as calcium channel blockers

IN Hu, Lain-Yen; Rafferty, Michael Francis; Ryder, Todd Robert

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 137 pp.

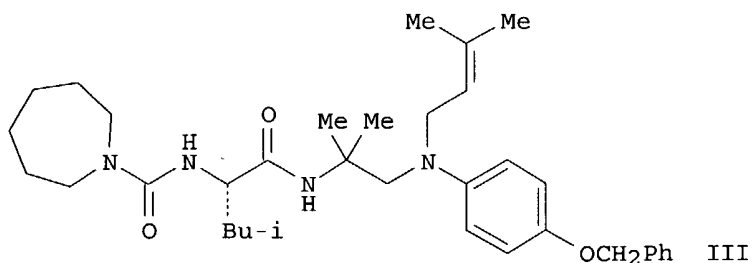
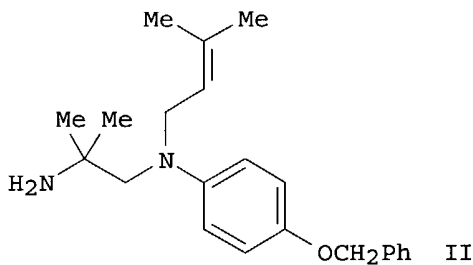
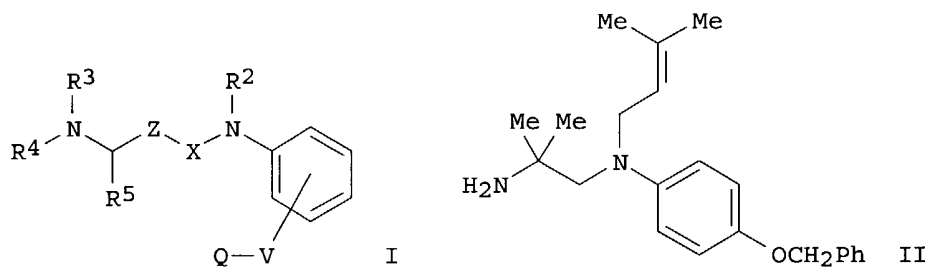
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|-----------------|----------|
| PI | WO 9907689 | A1 | 19990218 | WO 1998-US15907 | 19980729 |
| | W: | AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| | AU 9887627 | A1 | 19990301 | AU 1998-87627 | 19980729 |
| | ZA 9807144 | A | 19990510 | ZA 1998-7144 | 19980807 |
| | US 6251918 | B1 | 20010626 | US 1999-402196 | 19990929 |
| | US 2001023249 | A1 | 20010920 | US 2001-769798 | 20010125 |
| | US 6495715 | B2 | 20021217 | | |
| | US 2003060632 | A1 | 20030327 | US 2002-252854 | 20020923 |
| PRAI | US 1997-55251P | P | 19970811 | | |
| | US 1998-82358P | P | 19980420 | | |
| | WO 1998-US15907 | W | 19980729 | | |
| | US 1999-402196 | A3 | 19990929 | | |
| | US 2001-769798 | A3 | 20010125 | | |
| OS | MARPAT 130:196584 | | | | |
| GI | | | | | |



AB The invention provides compds. that block calcium channels. In

particular, the invention claims compds. I [Z = CH₂ or CO; X = cycloalkylene, (un)substituted heterocycloalkylene, imino or iminoalkylene, certain piperidinediyl or pyrrolidinediyl radicals or their alkylene derivs.; Q = H, (un)substituted aryl, heteroaryl, cycloalkyl, alkyl, heterocycloalkyl; V = O(CH₂)_n or (CH₂)_nO, O, (CH₂)_n, CH:CH, NH(CH₂)_n or (CH₂)_nNH or derivs.; R₂ = H, alkenyl, cycloalkenyl, (un)substituted Ph, alkyl, cycloalkyl, or Ph; R₃ = H, alkyl, alkenyl; R₄ = H, cyclo-(CH₂)_mNCO, alkyl, alkenyl, (un)substituted Ph, heteroaryl, or cycloalkyl; or NR₃R₄ = 5- to 7-membered ring with an optional addnl. heteroatom; R₅ = alkyl, (un)substituted Ph or heteroaryl; m = 1-3; n = 0-3] and their pharmaceutically acceptable salts, esters, amides, and prodrugs. The invention also provides methods of using the compds. to treat stroke, cerebral ischemia, head trauma, or epilepsy, and to pharmaceutical compns. that contain the compds. Over 50 synthetic examples are given, and these plus a large number of addnl. invention compds. are specifically claimed. For instance, N-BOC-α-aminoisobutyric acid underwent amidation with 4-benzyloxyaniline, followed by reduction of the amide with diborane, N-alkenylation with 4-bromo-2-methyl-2-butene, and acidic deprotection to remove BOC, to give intermediate II. In a sep. preparation, H-Leu-OCH₂Ph was treated with triphosgene and hexamethylenamine, then deprotected, to give Hac-Leu-OH (III; Hac = hexamethylenaminocarbonyl). Coupling of II with III using HBTU and DIPEA in DMF gave title compound IV. The latter blocked calcium flux through N-type Ca²⁺ channels in IMR-32 neuronal tumor cells in vitro, with IC₅₀ of 0.26 μM. Selected compds. gave 20-100% protection of mice from tonic seizures in a sound chamber, at doses of 10-30 mg/kg i.v.

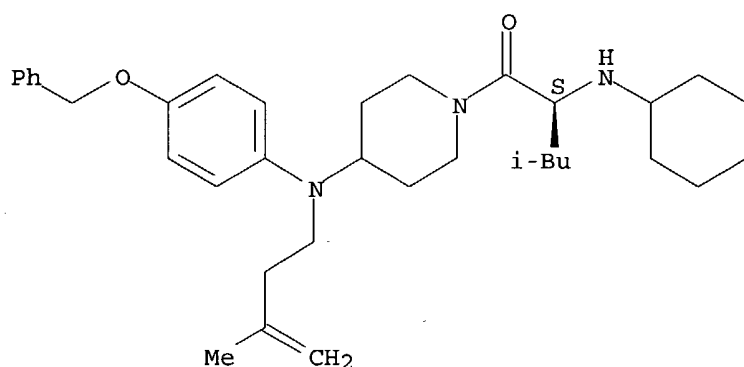
IT 220737-62-2P 220738-14-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aniline derivs. as calcium channel blockers)

RN 220737-62-2 CAPLUS

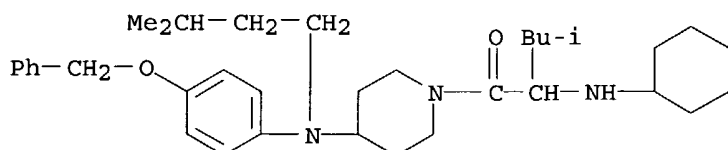
CN 4-Piperidinamine, 1-[(2S)-2-(cyclohexylamino)-4-methyl-1-oxopentyl]-N-(3-methyl-3-butenyl)-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220738-14-7 CAPLUS

CN 4-Piperidinamine, 1-[2-(cyclohexylamino)-4-methyl-1-oxopentyl]-N-(3-methylbutyl)-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT